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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,125	09/11/2003	Mark Robert Cobain	T3089(C)	6912

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,125	COBAIN ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-10* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed January 3, 2006 is acknowledged and has been entered.

Election/Restrictions

1. Newly submitted claim 10 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 10 involves selecting a population of individuals and the originally filed claims do not require this limitation. Claim 10 requires determining a perceived stress scale score for each individual by administering a perceived stress scale questionnaire and claim 1 does not require this limitation. Claim 10 requires a subpopulation having a perceived stress scale score and Claim 1 does not require this limitation.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 10 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1 and 5-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification on page 2, lines 3-35 discloses that the presence of psychological stress or increased psychological stress levels can be identified by an increase in the level of one or more isoprostanes. The specification on page 13, Example 2 through page 18, line15 discloses giving a questionnaire to participants and dividing the sample into low stress and high stress groups and comparing the results of the two groups. The specification on page 17, lines 24-25 discloses that correlations between urinary isoprostanes and cortisol secreted during stress period for both "stress" and "control groups". The applicant does not disclose calculating the psychological stress level from the measured isoprostane level by determining statistically greater isoprostane levels compared with the measured average isoprostane level obtained from a control group assessed to have low psychological stress. There is no description in the specification disclosing calculating the psychological stress level from the measured isoprostane level by determining statistically greater isoprostane levels compared with the measured average isoprostane level obtained from a control group assessed to have low psychological stress.

4. Claims 1 and 5-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the detection of isoprostanes in a biological sample derived from a human, does not reasonably provide enablement for a method of diagnosing a psychological stress level in a human. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method of determining a psychological stress level in a human, the method comprising with measurement means, measuring the level of one or more isoprostanes in a biological sample derived from the human and calculating the psychological stress level from the measured isoprostane level by determining statistically greater isoprostane levels compared with the measured average isoprostane level obtained from a control group assessed to have low psychological stress. The specification on page 2, lines 3-35 discloses that the presence of psychological stress or increased psychological stress levels can be identified by an increase in the level of one or more isoprostanes. The specification on page 13, Example 2 through page 18, line15 discloses giving a questionnaire to participants and dividing the sample into low stress and high stress groups and comparing the results of the two groups. The specification on page 17, lines 24-25

discloses that correlations between urinary isoprostanes and cortisol secreted during stress period for both "stress" and "control groups". Page 18, lines 8-13 disclose that the demonstration that reported perceived stress correlates with the isoprostane levels, and their metabolites, found in urine, and the observation that stress reactivity, as indexed by cortisol secretion occurring during a stress period, is related to the base level of isoprostanes produced indicates that isoprostanes and stress are related.

However, the specification does not clearly teach what is involved in psychological stress. Further, the specification does not appear to teach a method of diagnosing a psychological stress level in a human. Although, the specification compares cortisol levels of saliva with urine isoprostanes, the specification does not positively teach diagnosing a psychological stress level in a human by measuring isoprostanes. Nor does the specification disclose a threshold or normal values for patients. Also, although the specification teaches dividing a sample of patients which have taken a questionnaire into two groups of low stress and high stress groups and teaches comparing these to groups to each other, the specification does not positively teach diagnosing a psychological stress level in a human by measuring isoprotane levels. Further, it is unclear what is considered to be statistically greater levels of isoprotane. Further, according to Taber's Cyclopedic Medical Dictionary, the amount of stress humans can withstand without having a pathological reaction to it varies from individual to individual and from situation to situation.

The specification only teaches comparing cortisol levels of saliva with urine isoprostanes and also teaches comparing urinary isoprostane levels of low stress

groups to urinary levels of high stress groups. It does not provide any guidance of determining a isoprotane level in a patient and comparing to a normal group of patients and determining a statistically greater isoprotane level to diagnose a psychological stress level.

Also according to Strongin (Laboratory Diagnosis of Viral Infections, Sensitivity, Specificity, and Predictive Value of Diagnostic Tests: Definitions and Clinical Applications, Lennette, e., ed., Marcel Dekker, Inc., New York, pp.211-219, 1992) a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics include the following: (1) the sensitivity of the assay; (20 the true-positive test rate: (3) the false-negative test rate; (4) the specificity, or percentage of patients without the disease who will display a negative result; (5) the true-negative test rate; (6) the false-positive test rate; (7) the predictive value, or the probability that the test result is correctly indicating the presence or absence of the disease; (8) the prevalence, or number of patients in any given population that have the disease in question; (9) the efficiency or percentage of all results that are true; (10) the accuracy of the recited diagnostic assay.

Additional consideration must also be examined to enable the clinician to practice the invention, including assessment of the following: (1) when is the maximum sensitivity desired? (2) when is the maximum specificity desired?; (3) when is the maximum efficiency desired?; (4) how is the maximum sensitivity or specificity achieved?; (5) how is the predictive value maximized? An essential understanding of

these factors is required to enable the skilled artisan to accurately use and interpret any given diagnostic test.

Because of the lack of description in the specification to diagnose a psychological stress level in a human as claimed or teach any information regarding the patients from which the samples were taken, and whether any consideration were given to the disease prevalence, predictive value, efficiency, or accuracy of the recited diagnostic assay, nor does applicant define what is considered to be statistically greater isoprostane levels, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1 and 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step of obtaining a biological sample from the human and also a step of contacting the antibodies directed to the isoprostanes with the sample. Further, method claims should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing, reacting, and detecting. Method claims should also clearly state each component used in the method and the relationship of the various components, and should not be a mere cataloging of

parts. The claims should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim.

Claim 1 the recitation "the one or more fluids" there is insufficient antecedent basis for this limitation.

Claim 1 is vague and indefinite because it is unclear what applicant intends by reciting a second bodily fluid "one or more fluids". In the method, what relationship exits between the first body fluid and the second body fluid? Is the second body fluid collected at the same time or a different time? Is the second body fluid the same type or different from the first biological fluid? Is a correlation established between the first and second biological fluids to determine psychological stress? Does the isoprostanes have to be increased in both fluids to indicate psychological stress? Does an increase in only one of the fluids indicate psychological stress? It is unclear what applicant intends or is trying to encompass.

Claim 1, line 7 the recitation "to each human" is vague and indefinite because it is unclear what applicant intends. Line 2 of claim 1 recites "a human" which insinuates a single human. Are there more than one human being tested? Which humans is applicant referring to? Is applicant collecting fluids from more than one human to determine the psychological stress in the human? What does applicant intend?

Claim 1, line 8 the recitation "statistically greater" is vague and indefinite. It is unclear what is considered to be statistically greater. There is not definition provided for the term in the specification. Is one, two, three or four standard deviations considered

to be "statistically greater"? Is 1%, 10%, 25% or 60% above the low psychological stress considered to be "statistically greater"? Is a mere increase compared to the low psychological stress considered to be "statistically greater"?

Claim 1, line 10 the recitation "low psychological stress" is vague and indefinite. It is unclear what is considered to be low psychological stress.

Claim 5 is vague and indefinite because it is unclear how psychological stress is "associated with" one or more conditions. It is unclear if applicant is merely stating that psychological stress is related to the recited disorders or if applicant is trying to diagnose the recited disorders. It is unclear what applicant is trying to encompass.

Response to Arguments

7. Applicant's arguments filed January 3, 2006 have been fully considered but they are not persuasive.

Applicant argues that claim 1 has been amended to recite that the psychological stress level is measured from the measured isoprostane level by comparing the measured isoprostane level with isoprostane levels obtained from a control group assessed to have a low psychological stress. Applicant states that this is based on the aforementioned passage in Example 2. This is not found persuasive because it is unclear what is considered to be statistically greater isoprotane levels (see rejections above) and further because Example 2 is merely providing a questionnaire and dividing perceived stress scores into two groups: 1) low stress group and 2) high stress group and then comparing urinary isoprostanes in the two groups. Applicant has not set normal values, nor has applicant defined what is considered to be statistically greater

isoprostane levels. Example 2 is comparing two stressed groups and also comparing urinary isoprostanes with cortisol levels.

Applicant agues that claim 1 has been amended to include the step of obtaining a sample. This is not found persuasive because there is no positive step recited in claim 1 of obtaining a sample.

Applicant argues that a person of ordinary skill in the art would readily appreciate how to measure the antibody or antibody fragments in more than one fluid to obtain separate indications of psychological stress and to average them to enhance overall accuracy. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., measure the antibody or antibody fragments in more than one fluid to obtain separate indications of psychological stress and to average them to enhance overall accuracy) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With respect to claim 5, Applicant argues that from the tenor of the specification, it is merely the psychological stress level which is being measured and correlations between the psychological stress level and the condition being examined. This is not found persuasive because limitations from the specification are not read into the claims. Further, it is unclear how the conditions are associated with psychological stress.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
March 20, 2006

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03/31/06